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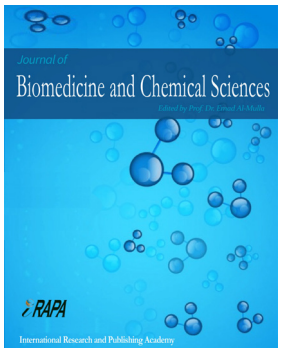

Quantification Assay of Diabetic Drug Sitagliptin in Pharmaceutical Preparations: A Review

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ABSTRACT

The diabetic drug Sitagliptin (STG) is a hypoglycemic drug of the dipeptidyl peptidase-4(DPP-4) inhibitor. The new therapeutic action by DPP-4 inhibitors depends on the decrease of the glucagon levels and stimulates glucose-dependent insulin release. This is done through inhibition of the inactivation of incretins, particularly glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), thereby improving glycemic control. Quantification Assay of STG in pharmaceutical preparations is one of the researchers' interests because of its importance in the manufacturing of drugs, quality control of the dosage forms, and the accuracy in determining the dose. However, in biological fluids, determination of the drugs is of greater importance, as monitoring the drug, studying its pharmacokinetics, bioavailability, potency, the chemical and biological actions of the drugs and their metabolites in the body. This is a review of STG, its properties, action, and methods of determination.

INTRODUCTION

Sitagliptin phosphate monohydrate (STG) is 1,2,4-triazolo [4,3-a] pyrazine,7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl) butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl) phosphate mono hydrate. It is classified as heterocyclic nitrogen compounds, with functional primary aliphatic amine group and electron withdrawing groups (Fluorides) (Sekaran & Rani, 2010). Figure 1 show the chemical structure of STG.

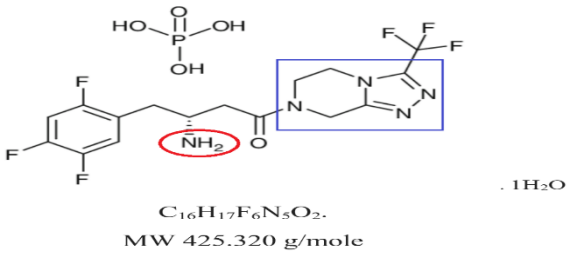

Fig. 1. The chemical structure, the chemical formula, and the molar mass of STG

STG appears as white non hygroscopic crystalline, non-hygroscopic, soluble in water and N, N-dimethylformamide, slightly soluble in methanol and very slightly soluble in ethanol, acetone and acetonitrile (Sirigiri, et al., 2018). STG is orally administrated as a hypoglycemic drug of the dipeptidyl peptidase-4(DPP-4) inhibitor. The new therapeutic action by DPP-4 inhibitors depends on decrease of the glucagon's levels and stimulate glucose-dependent insulin release. This is done through inhibition of the

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inactivation of incretins, particularly glucagon-like peptide-1 (GLP-1) and gastric inhibitory polypeptide (GIP), thereby improving glycemic control (Nirogi, et al., 2008; Anderson, 2018). Figure 2 shows this mechanism.

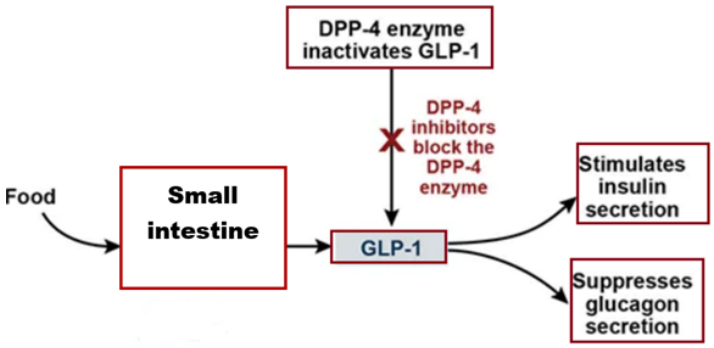

Fig. 2. The mechanism of action of 4(DPP-4) inhibitor

STG was approved in October 2006 by the U.S. Food and Drug Administration (FDA), and is marketed in the USA as a brand name Januvia (Hirshberg & Raz, 2011). The common side effects of STG are headaches, upper respiratory tract infections, and swelling of the legs, high dose may cause in angioedema, kidney problems, low blood sugar, joint pain, and pancreatitis as a side effect (Nirogi, et al., 2008).

I.R. spectrum (Figure 3) shows the basic functional groups carbonyl and amine as well as other structural details, band at 1639.96 cm $^{-1}$ due to the carbonyl group and at 3324.50 cm^{-1}refer to NH_2 group at about 3300 cm^{-1} adjacent to the band at 3032cm^{-1} refer to NH, 2361 cm^{-1}refer to CN triple bonds,1636 cm^{-1}refer to the carbonyl, 1525 cm^{-1} may be due to aromatic. The spectrum of uv shows a clear maximum at 268nm. (Figure 4) (Shantikumar, et al., 2014).

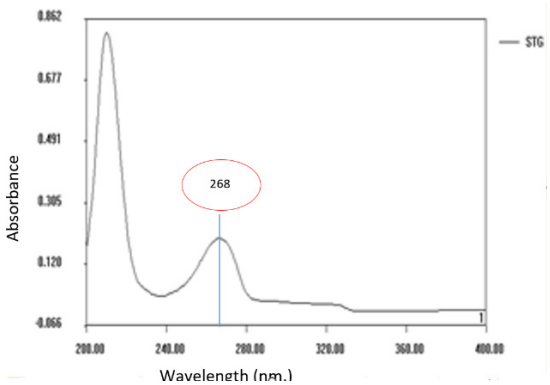

Fig. 3. The spectrum of STG at UV region

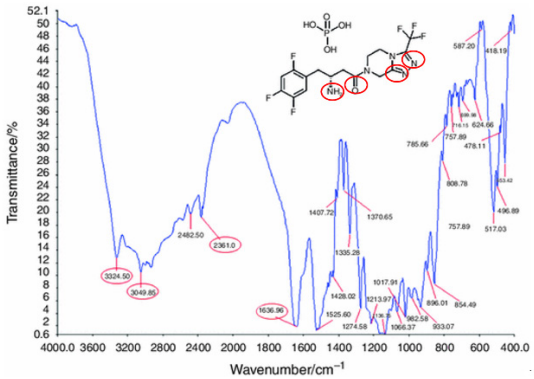

Fig. 4. The spectrum of STG at I.R. region

STG has been determined in tablet dosage forms by spectrophotometric methods at UV. The drug shows maximum absorption at 267 nm in water with linear response over the concentration range of 2-10 µg /ml. The correlation coefficient was 0.9995. The recovery was ranged from 99.53to 100.41 with good precision in which RSD% was less than 2.0 % (Ravisankar, et al., 2014). Spectrophotometric methods based on measuring the intensity of the formed color at visible region; one of these methods was based on the charge

transfer reaction with 2, 3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), 7,7,8,8-tetracyanoquinodim ethane (TCNQ) and tetrachloro-1,4-benzoquinone (p-chloranil). Many variables were studied to select the best reaction conditions. Beer's law was obeyed from 50 to 300, 20 to120, and 100-900 µg/ml with DDQ, TCNQ and p-chloranil, respectively (El-Bagary, et al., 2011). STG was determined by other method based on the oxidative coupling with 3-methyl-2-benzthiazolinone hydrazine (MBTH) to form green in color exhibits maximum absorbance wave at 612 nm. The linearity according to Beer's law was 1–18 µg/ml. The statistical f and t-test shows high validation of the method (Disha & Gurupadhayya, 2015).

An accurate, sensitive and novel reverse phase high performance liquid chromatographic method (RP-HPLC) has been developed for the assay of STG Phosphate in the pharmaceutical dosage form. The chromatographic separation of STG was achieved by the rmoscientific C_{18} column, (250x4.6 particle size of 5µ) at room temperature and UV detection at 248 nm. Methanol was used as a mobile phase with isocratic elution mode at a flow rate of 1ml/min. The retention time R_f of STG was 1.91min (Sireesha & Sravya, 2017). A Reported high HPLC procedure was followed for estimating STG phosphate monohydrate. The method was eco-friendly the drug in the presence of metformin hydrochloride (MET) by using of Shimadzou® C_{18} column (250mm × 4.6mm, 5µm). The elution was achieved by acidified water and methanol in the ratio of 60:40 (v/v) as mobile phase at a flow rate of one ml /min. The peaks were detected at 260nm with retention time for MET and STG were 1.96 and 3.70 min, correspondingly. Many variants were studied to select the optimum chromatographic conditions of analysis; the linearity, limit of detection (LOD), limit of quantification (LOQ), accuracy, precision, robustness, specificity, and validation according to ICH Guidelines were calculated. with the reported methods (Raza, et al., 2022).

A rapid and sensitive HPLC method combined with fluorescence detector for estimation of STG mono phosphate in human plasma. The drug was extracted by liquid-liquid procedure using ethyl acetate. 0.01M phosphate buffer (pH 4.5) and acetonitrile were used as a mobile phase in a ratio 73:27 pumped reversely at flow rate 1 ml/min and detected at 267 nm. The validation was followed over a range of concentration from 0.1 to 3 µg/ml for STG according to FDA guidelines. The intraday and inter-day precision were less than 5% and accuracy was ranged from 90 to105% (Ahmed, et al., 2018). RP-HPLC for the assay of STG Phosphate in tablet dosage forms was developed by the stationary phase Qualisil C BDS column with the internal diameter of 150×4.5mm, 5µ. The mobile phase consists of potassium dihydrogen phosphate (pH 4.5) and acetonitrile in the ratio of 60:40 (v/v). The flow rate was 1.0ml/min, R_f of STG phosphate monohydrate was 2.70min detected at 228nm. (Patil, et al., 2010). STG was also determined in pharmaceutical dosage form HPLC using Cosmosil C_{18} (250mm 4.6mm, 5mµ particle size) and UV detection at 255nm. An isocratic mobile-phase methanol: water (70:30) was pumped with a flow rate of 0.8ml/min. a validation according to ICH guidelines was calculated. The linearity 10-50 µg/ml. Limit of identification, the limit of quantification, accuracy, precision, and robustness of the determination were all calculated (Singh, et al., 2022).

A simultaneous estimation of Saxagliptin and STG in bulk and tablet dosage form was carried out by chromatography using Std Discovery C_{18} of 150 x 4.6 mm.as the inner diameter and 5µm particle size. The mobile phase consists of 0.1% ortho phosphoric acid OPA (2.2pH): acetonitrile (60:40) and the flow rate was 1 ml/min. pumped to column at 30°C. The selected wavelength was 218 nm. for STG and 255 nm. for Sitagliptin. STG was retained at time 2. 880min.The method was precise (RSD% = 0.7%) and very accurate (Recovery% 100.01%), LOD, and LOQ of STG was 0.61 and 1.40 µg/ml (Rajeswari, et al., 2022). A simultaneous determination of STG and Irbesartan (IRB) by LC-MS/MS method was used for the bioanalytical determination of both drugs in the dosage forms and the biological samples for the study of drug-drug interactions (STG and IRB). The column used was YMC triart C_{18} with the inner diameter of 50 mm × 4.6 mm and 3 µm particle size, the drugs were separated using a gradient elution (the run time was 5 min.), the flow rate was 1 ml/min. A multiple reaction monitoring was followed and detected by mass technique. The method was able to determine from 5 to1000 ng/ml, for both drugs. The recovery% for STG of inter and intra within-batch and between-batch was ranged from 98.4 to107.2% for STG, and from 92.4 to102.5% for IRB (Bhargavi, et al., 2023). STG was estimated by a fluorescence technique selectively depending on its properties., excipients in the pharmaceuticals exhibits no while determination of STG in urine samples requires solid-phase extraction (de Paula e Mancilha, et al., 2013).

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Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Competing Interest

The authors had no competing interests.

REFERENCES

[1] Ahmed, R. M., Hadad, G. M., El-Gendy, A. E., & Ibrahim, A. (2018). Development of HPLC method for determination of sitagliptin in human plasma using fluorescence detector by experimental design approach. *Analytical Chemistry Letters, 8*(6), 813-828. https://doi.org/10.1080/22297928.2018.1545603

[2] Anderson, P. O. (2018). Treating diabetes during breastfeeding. *Breastfeeding Medicine, 13*(4), 237-239. https://doi.org/10.1089/bfm.2018.0036

[3] Bhargavi, P. D., Lolla, S., Sugunan, S., Gubbiyappa, K. S., Khan, A. A., Alanazi, A. M., & Nayak, B. V. (2023). The simultaneous quantification of Sitagliptin and Irbesartan in rat plasma using the validated LC-MS/MS method is applied to a pharmacokinetic study. *Journal of Chromatography B, 1221*, 123677. https://doi.org/10.1016/j.jchromb.2023.123677

[4] de Paula e Mancilha, T., de Paula, C. E. R., Cassella, R. J., & Pacheco, W. F. (2013). Direct determination of sitagliptin in pharmaceutical formulations and its determination in urine after solid-phase extraction by sp ectrofluorimetry. *Luminescence, 28*(6), 873-878. https://doi.org/10.1002/bio.2449

[5] Disha, N. S., & Gurupadhayya, B. M. (2015). Spectrophotometric determination of Sitagliptin phosphate in bulk and pharmaceutical formulations. *International Journal of Innovative Science, Engineering and Technology, 2*(7), 702-709.

[6] El-Bagary, R. I., Elkady, E. F., & Ayoub, B. M. (2011). Spectrophotometric methods for the determination of sitagliptin and vildagliptin in bulk and dosage forms. *International Journal of Biomedical Science: IJBS, 7*(1), 55. https://pubmed.ncbi.nlm.nih.gov/23675221/

[7] Hirshberg, B., & Raz, I. (2011). Impact of the US Food and Drug Administration cardiovascular assessment requirements on the development of novel antidiabetes drugs. *Diabetes Care, 34*(Suppl 2), S101. https://doi.org/10.2337/dc11-s202

[8] Nirogi, R., Kandikere, V., Mudigonda, K., Komarneni, P., Aleti, R., & Boggavarapu, R. (2008). Sensitive liquid chromatography tandem mass spectrometry method for the quantification of sitagliptin, a DPP-4 inhibitor, in human plasma using liquid–liquid extraction. *Biomedical Chromatography, 22*(2), 214-222. https://doi.org/10.1002/bmc.926

[9] Patil, S., Ramesh, B., Hareesh, A. R., Patil, K., & Dhokane, A. (2010). Development and Validation of RP-HPLC Method for the Estimation of Sitagliptin Phosphate in Tablet Dosage Form. *Asian Journal of Research in Chemistry, 3*(3), 653-655.

[10] Rajeswari, A., Saritha, N., & Devanna, N. (2022). Validated RP-HPLC Method Development for Estimation of Ertugliflozin and Sitagliptin in Bulk and Dosage Forms. *Journal of Pharmaceutical Research International, 34*, 22-26.

[11] Ravisankar, P., Mounika, G., Devadasu, C., & DevalaRao, G. (2014). A simple validated UV Spectrophotometric method for quantitative analysis of Sitagliptin phosphate in pharmaceutical dosage form. *J. Chem. Pharmaceut. Sci, 7*, 254.

[12] Raza, A., Murtaza, S. H., Hanif, S., Iqbal, J., Ali, I., Aftab, T., ... & Syed, M. A. (2022). Validation of a rapid and economical RP-HPLC method for simultaneous determination of metformin hydrochloride and sitagliptin phosphate monohydrate: Greenness evaluation using AGREE score. *Pakistan Journal of Pharmaceutical Sciences, 35*(1).

[13] Sekaran, C. B., & Rani, A. P. (2010). Development and validation of spectrophotometric method for the determination of DPP-4 inhibitor, sitagliptin, in its pharmaceutical preparations. *Eclética Química, 35,* 45-53. https://doi.org/10.1590/S0100-46702010000300003

[14] Shantikumar, S., Sreekanth, G., SurendraNath, K. V., JaferValli, S., & Satheeshkumar, N. (2014). Compatibility study between sitagliptin and pharmaceutical excipients used in solid dosage forms. *Journal of Thermal Analysis and Calorimetry, 115*, 2423-2428. https://doi.org/10.1007/s10973-013-3329-3

[15] Singh, D., Jain, N. K., Tiwari, A., & Khan, N. (2022). Development and Validation of Simultaneous Equation Method for Estimation of Sitagliptin and Saxagliptin in Combined Pharmaceutical Dosage Form by Using UV Spectrophotometric Method. *International Journal of Medical Sciences and Pharma Research, 8*(2), 83-90. https://doi.org/10.22270/ijmspr.v8i2.43

[16] Sireesha, D., & Sravya, E. (2017). Development and validation of RP-HPLC method for the estimation of sitagliptin phosphate in tablet dosage form. *International Journal of Applied Pharmaceutical Sciences and Research, 2*(03), 41-45. https://doi.org/10.21477/ijapsr.v2i3.8099

[17] Sirigiri, N., Subramanian, N. S., Reddy, G., & Kumar, N. (2018). Stability indicating method development and validation for simultaneous estimation of sitagliptin phosphate and metformin HCl in tablets by HPLC. *International Journal of Pharmaceutical Sciences and Research, 9*(10), 4294-430